Maryland Department of Health and Mental Hygiene
Laboratories Administration

Bioterrorism Newsletter

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The Role of the Clinical Laboratory in Preparedness and Response to Bioterrorism

In recent years there has been a rise in the number of bioterrorism incidents in the United States, and almost all of them have proved to be hoaxes. Most of these have involved threats of an anthrax release. In 1997, Congress addressed the threat of terrorism by enacting legislation and providing funds to build the public health infrastructure to develop the capacity to respond to threats and actual terrorist events. ***The U.S. Department of Health and Human Services (HHS)*** was given the responsibility for bioterrorism attacks on the civilian population. The Department of Health and Human Services has designated the ***Centers for Disease Control and Prevention (CDC)*** to coordinate and lead the overall planning to upgrade national public health capabilities of responding to biological and chemical agent terrorism.

What is bioterrorism? Bioterrorism is the intentional use of microbial agents, their toxins, or chemical products to harm individuals or populations. A bioterrorism attack may be politically motivated or motivated by personal reasons. Public health response to bioterrorism includes detection of the event (Health Surveillance), rapid laboratory diagnosis of the agent, epidemiologic investigation, and implementation of control measures. Agents most likely to be used by a terrorist are those that are not endemic or typically present in the community. Practitioners need to familiarize themselves with the clinical present–ations of these agents. Level A clinical laboratories will need to have procedures in place to rule out these agents and refer suspected isolates to the state public health laboratory. Once a suspect agent is identified, it should be referred immediately to the public health laboratory to confirm the initial identification.

Biological threat agents under current consideration are *Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, *Brucella spp*, *Clostridium botulinum*, *Variola major* (smallpox virus), and viral hemorrhagic fevers. These agents are referred to as select biological agents. Routes of exposure most likely to be used for these agents are inhalation by aerosols and ingestion of contaminated food or water.

On April 21, 2000, the ***CDC*** published a Strategic Planning Workgroup report on ***"Preparedness and Response to Biological and Chemical Terrorism: A Strategic Plan."*** The strategic plan is based on five focus areas: Preparedness and Prevention, Detection and Surveillance, Diagnosis and Characterization of Biological and Chemical Agents, Response, and Communication. The plan calls for state and local health care agencies to investigate unusual events and unexplained illnesses, and for diagnostic laboratories to be equipped to identify biological and chemical agents. The plan also calls for the creation of a multilevel laboratory response network linking clinical laboratories to public health agencies in all states and local areas and to facilities that can analyze biological agents. Implementing the plan by 2004 will ensure that the national laboratory response network for bioterrorism include facilities in all 50 states.

A bioterrorism event may be either overt or covert. An overt event is usually announced by the perpetrator to create fear and disrupt normal operations. Therefore, these events are

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recognized very early and the response is immediate. The police department and fire department are first responders, followed by the FBI, to gather evidence and attempt to find the perpetrators. A covert event is unannounced and the first evidence may be cases of infection appearing in hospital outpatient departments, hospital admissions and physicians' offices. The disease outbreak will first appear as a natural outbreak, and will require epidemiologic and laboratory investigation to determine if the outbreak is the result of a terrorist attack. Recognition of the outbreak will emerge slowly and the response will be delayed. Appropriate treatment may also be delayed until the infectious agent is isolated and identified. Characterization of the infectious agent by gene sequencing may help to distinguish the naturally occurring agent from a laboratory-derived strain or a genetically derived strain. The first responders are health care workers, and early recognition of the agent will assist these workers to use appropriate protective measures.

A national laboratory response network was established by CDC and the Association of Public Health Laboratories to develop the infrastructure needed to respond to bioterrorist threats. Laboratories are classified at four levels, based on their capacity to identify the common biological threat agents.

Level A consisits primarily of hospital laboratories that would be first responders to cover a bioterrorist event. These laboratories are expected to rule out or refer to the public health laboratory the select biological agents. If a select biological agent is detected and identified, it should still be referred to both the public health laboratory for genetic characterization and to the national collection center for these agents.

Level B is primarily made up of public health laboratories, which will rule-in the select agents and refer to level C laboratories. These laboratories have biosafety level II and biosafety level III facilities.

Level C contains advanced, large public health laboratories with biosafety level III facilities and the genetic technology and typing tests to rule-in biological agents. These agents are retained in stock cultures for future reference and for development of more rapid methods of identification, as well as for referral of these biological agents to the national collection center at CDC.

Level D are federal laboratories located at CDC and USAMRIID which have biosafety level IV facilities to study highly infectious viral agents, such as those casuing smallpox and hemorrhagic fevers. These facilities are responsible for developing new tests and technologies, and maintaining stock agents referred by state public health laboratories. Federal laboratories provide training, procedures, and reagents to the state public health laboratories and assist them in conducting training for level A laboratories and other agencies responsible for responding to bioterrorism.

Referral of Microorganisms

Level A laboratories are requested to refer all specimens and microorganisms that may represent one of the select bioterrorism agents to the DHMH Laboratories Administration for further characterization. All such agents will be retained in a culture collection for later reference in developing improved and rapid detection technologies. These agents will also be sent to the CDC for the national culture collection, to be used for a similar purpose.

Other examples of laboratory findings that should be referred to the DHMH Lab–oratories Administration are the following:

1. If gram-positive bacilli are isolated from sputum and/or blood culture from patients with pulmonary disease, the isolate should not be discarded as a contaminant but referred to the Laboratories Administration for further characterization to

eliminate *Bacillus anthracis*. If the Level A laboratory identifies the bacillus as a non-pathogenic strain, the isolate need not be referred.

2. If gram-negative coccobacilli are isolated from sputum and/or blood culture from patients with pneumonic disease, the isolates should not be discarded but referred to the Laboratories Administration, unless the Level A laboratory is certain the identify of the isolate is other than a select biological agent.

3. If gram-negative coccobacilli or bacilli are observed in a gram-stained smear but fail to grow in culture, a portion of the specimen should be referred to the Laboratories Administration. This condition may occur where the lab is not using special media required for the isolation of fastidious microbes such as *Francisella tularensis*.

Storage of Select Agents

Proper storage of select agents is absolutely essential to restrict access to these agents. It is recommended that they be kept in locked storage with only a few key laboratory staff having access. A record of stored agents should be kept and an inventory taken periodically to enable the Laboratory Director to determine if any stock cultures are missing. When cultures are missing and the circumstances cannot be resolved, the Laboratories Administration should be notified promptly to be alerted about the missing stock culture.

What do Laboratory Directors Need to Do Now?

Review safety procedures to determine if the laboratory could safely handle an initial culture and identification of threat agents, review testing procedures to determine if they are consistent with recommended identification schemes, assure that appropriate packaging is available for the transport of culture/specimens, and contact the **State Public Health Laboratory** to become integrated into the Stat's response planning (call **410-767-6100**).

Collaborations formed during development of the national bioterrorism response network will be equally valuable in strengthening the State's surveillance and control of endemic and emerging infectious diseases. Preparation and planning are necessary so that if an attack does occur, microbiologists will be able to rapidly identify the probable, priority biological agents.

Clinical laboratories are the sentinels for bioterrorism and may be the first to see an organism in a covert attack, such as *Bacillus anthracis* in a blood culture or *Yersinia pestis* in sputum culture. The diagnostic microbiology laboratory staff should have uniform procedures and training and be able to recognize bioterrorism agents. They must know what to send for further testing and who to send it to, and must know if there are any special safety considerations for this testing. The Laboratories Administration can provide guidance on these issues.

Level A laboratories need to know the following information:

- Their role as a Level A laboratory.
- How to rule-out possible bioterrorism agents as quickly as possible.
- How to appropriately send potential bioterrorism agents to the State Public Health Laboratory *immediately* to rule-out or rule-in an agent.
- The safety devices needed to protect your staff when working with these agents.

Laboratories Administration

The DHMH Laboratories Administration has expanded its capacity to rapidly identify the select bioterrorism agents. Collaboration with Maryland hospitals and independent laboratories, to develop a network providing access to this testing methodology, is just beginning. Along with various State agencies, the Maryland Department of Health and Mental Hygiene is actively engaged in providing laboratories with background information about bioterrorism preparedness and response. Each issue of this quarterly ***Bioterrorism Newsletter*** will describe the role of the laboratory network and give pertinent information about biological agents, detection methods, and safety precautions. Plans are under way to develop a hands-on workshop for the important biological agents, so that all participants are able to recognize unusual microorganisms and take appropriate action. Other workshops are planned to inform the laboratory community about the State planning that is taking place, the participating agencies, and the roles of each member of the bioterrorism network. ☣